

## REMARKS

### **Claims**

Claims 1-13 are pending.

### **35 USC §102(b) rejection**

Claims 1-13 are rejected as allegedly being anticipated by Lexow (WO0161036A2). Applicant respectfully disagrees. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." See MPEP §2131 citing *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Generally, Lexow et al. describes a method of mapping restriction endonuclease cleavage sites and determining the nucleic acid sequence between the cleavage sites of a target protein using microarray, which in essence is a method of cutting up nucleic acids into smaller fragments so that they can be mapped. The disclosed method is illustrated in Figures 2 and 6 and described on pages 1, lines 30-37 carrying over to page 2, lines 1-30 and pages 11, lines 21-38, carrying over to page 12, lines 1-22. The method begins with a target nucleic acid molecule, whose nucleic acid sequence is to be mapped, and an array of other nucleic acids which are already immobilized to a solid support array. The target molecule is treated with a restriction endonuclease, which cuts the target molecule into multiple smaller fragments, called "Target DNA" in Figures 2 and 6. The target DNA fragments are then ligated to the already immobilized DNA array, termed overhang-adapters. The Target DNA-overhang-adapter complex is then cut with a restriction endonuclease and again ligated to an immobilized DNA array so that the Target DNA can be mapped. Here the starting material and the ending material, which is subsequently mapped, are both the identical nucleic acid sequence, known as "Target DNA", as described in Figures 2 and 6.

Specifically, Lexow et al. fails to anticipate claim 1 for the following reasons. Lexow et al. fails to teach step (d) "cutting ... thus releasing an elongated first at least partially double-stranded oligonucleotide." (emphasis added) On page 1, lines 27-34, Lexow teaches the cutting of a target nucleic acid molecule to be mapped, where the result is smaller nucleic acid fragments, which are called Target DNA in Figures 2 and 6. In addition, in Figure 2, Lexow teaches the cutting of the Target DNA-overhang-adapter complex, where the result is the exact same size Target DNA molecule from the previous steps. Lexow fails to teach the elongation of oligonucleotides, therefore, Lexow fails to anticipate the present claims.

In addition, Lexow et al. fails to teach claim 1 step (a) a modification allowing the first at least partially double-stranded oligonucleotide to be immobilised to a surface, and claim 1 step (b) a second modification allowing the second at least partially double-stranded oligonucleotide to be coupled to a surface. Claim 1 steps (a), (b), and (c) state:

“(a) providing a first at least partially double-stranded oligonucleotide, whereby the oligonucleotide comprises a first single-stranded overhang, and *a modification allowing the oligonucleotide to be immobilised to a surface, wherein the modification comprises a second single-stranded overhang,*

(b) providing a second at least partially double-stranded oligonucleotide, whereby the oligonucleotide comprises a recognition site for a first type IIS restriction enzyme which cuts outside its recognition site, *a modification allowing the oligonucleotide to be coupled to a surface* and a single-stranded overhang,

(c) ligating the first oligonucleotide and the second oligonucleotide via the first single-stranded overhang of the first oligonucleotide and the single-stranded overhang of the second oligonucleotide, generating a first ligation product, whereby the first ligation product comprises a modification allowing the first ligation product to be immobilised to a surface, wherein the *modification of the first ligation product essentially corresponds to the second single-stranded overhang of the first oligonucleotide ...*” (emphasis added).

Lexow teaches two oligonucleotides, the Target DNA and the overhang-adapter. See Figures 2 and 6. If the Examiner views the Target DNA as the claimed first oligonucleotide and the overhang-adapter as the second oligonucleotide, then steps (a), (b), and (c) of claim 1 are not met, as 1) the Target DNA, as shown in Figures 2 and 6, does not comprise a *modification allowing the oligonucleotide to be immobilised to a surface, wherein the modification comprises a second single-stranded overhang*; and 2) the ligation product, the Target DNA-overhang-adapter complex, does not comprise a modification that *essentially corresponds to the second single-stranded overhang of the first oligonucleotide* (Target DNA).

If the Examiner views the overhang-adapter as the claimed first oligonucleotide and the Target DNA as the second oligonucleotide then again steps (a), (b), and (c) of claim 1 are not met, as 1) the Target DNA, as shown in Figures 2 and 6, does not comprise a *modification allowing the oligonucleotide to be coupled to a surface*; 2) the Target DNA does not comprise a *recognition site for a first type IIS restriction enzyme*; and 3) the ligation product, the Target DNA-overhang-adapter complex, does not comprise a modification that *essentially corresponds to the second single-stranded overhang of the first oligonucleotide* (overhang-

adapter). As Lexow fails to teach the elements of claim 1 steps (a), (b), and (c), Lexow cannot be considered anticipatory.

In addition, the preamble of the claims, which reads a “method for the manufacture of a nucleic acid molecule” should be read as a limitation. The purpose of the claimed method, for manufacturing nucleic acids, gives life, meaning and vitality to the body of the claims. As shown by Lexow, many patent applications describing nucleic acids, include steps such as ligating and cutting, despite the fact that, as here, the prior art method and the claimed method are totally unrelated. Lexow teaches a method of cutting up target nucleic acids so that they can be mapped. Whereas, the present method is for the manufacture of nucleic acids, and requires the *elongation* of oligonucleotides in order to obtain a target nucleic acid. Here, the preamble clearly distinguishes the claimed method from the teachings of Lexow.

In summary, Lexow et al. fails to teach each and every element of the method of claim 1, therefore, cannot be considered to anticipate. Applicant respectfully requests the withdrawal of this rejection.

### **35 USC §102(e) rejection**

Examiner states that claims 13-21 are rejected, but the Applicant believes that claims 1-13 were intended, as only claims 1-13 are pending. Examiner alleges that US20060194202 recites a first oligonucleotide comprising a first and second overhang wherein one overhang comprises a modification and the other overhang participates in ligation. Applicant respectfully disagrees. As discussed in the reply filed by Applicant on 22 February 2011, US20060194202 describes the genus of modifications, but fails to teach that a modification can be the species of a single stranded nucleotide overhang. Examiner responds, in the present action, by citing page 17, paragraphs 0187-0188 as stating that the ligation product is immobilized to reaction wells via a modification in the transition anchor moiety, which indicates that the overhang sequence which participates in immobilization comprises a modification. Applicant will respectfully attempt to clarify. Examiner alleges that the overhang sequence comprises a modification, but this is not enough, as the claims require that the modification itself is a second single-stranded overhang, see specifically claim 1 step (a) “wherein the modification comprises a second single-stranded overhang” and step (c) “wherein the modification of the first ligation product essentially corresponds to the second single-stranded overhand of the first oligonuceleotide.” The unique claimed feature allows for immobilization to be reversed by increasing heat. As described, however, in paragraphs

0187-0188 and shown in Figure 5F, the modification is biotin, not a single stranded nucleotide overhang.

Neither the cited paragraphs nor the remainder of the specification of US20060194202 teach a modification allowing the oligonucleotide to be immobilised to a surface that comprises a single-stranded overhang, or a modification allowing the first ligation product to be immobilised to a surface that essentially corresponds to the same single-stranded overhang. As US20060194202 fails to teach or suggest all of the limitations of the present claims, the reference cannot be anticipatory. In view of the foregoing, Applicant respectfully requests that the Examiner withdraw the rejection.

## **CONCLUSION**

In view of the foregoing arguments/amendments, Applicant submits that the application is in condition for allowance. Should the Examiner feel that there are any issues outstanding after consideration of this response, the Examiner is invited to contact the undersigned to expedite prosecution of the application.

The Commissioner is hereby authorized by this paper to charge any fees during the entire pendency of this application including fees due under 37 C.F.R. §§1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-4520. **This paragraph is intended to be a CONSTRUCTIVE PETITION FOR EXTENSION OF TIME in accordance with 37 C.F.R. §1.136(a)(3).**

Respectfully submitted,

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